

NDA 11-795/S-016 & 11-459/S-035

AUG 30 2000

Pfizer, Inc.  
Regulatory Affairs Division  
Attention: Rita Wittich  
235 East 42nd Street  
New York, NY 10017-5755

Dear Ms. Wittich:

Please refer to your supplemental new drug application dated December 19, 1994, and December 28, 1994, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vistaril (hydroxyzine pamoate) Capsules and Oral Suspension

These "Changes Being Effected" supplemental new drug applications provide for addition of instructions for shaking, the suspension product in the HOW SUPPLIED section.

We have completed the review of these supplemental new drug applications and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling. Accordingly, the supplemental applications are approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you should have any questions, please call Anna M. Homonnay-Weikel, R.Ph., Regulatory Project Manager, at (301) 594-5535.

Sincerely,

Russell Katz, MD  
Director  
Division of Neuropharmacological Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

# VISTARIL®

(hydroxyzine pamoate)

Capsules and

Oral Susepension

## DESCRIPTION

Hydroxyzine pamoate is designated chemically as 1-(p-chlorobenzhydryl) 4- [ 2- (2-hydroxyethoxy) ethyl] diethylenediamine salt of 1,1'- methylene bis (2 hydroxy-3-naphthalene carboxylic acid).

Inert ingredients for the capsule formulations are: hard gelatin capsules (which may contain Yellow 10, Green 3, Yellow 6, Red 33, and other inert ingredients); magnesium stearate; sodium lauryl sulfate; starch; sucrose.

Inert ingredients for the oral suspension formulation are: carboxymethylcellulose sodium; lemon flavor; propylene glycol; sorbic acid; sorbitol solution; water.

## CLINICAL PHARMACOLOGY

Vistaril® (hydroxyzine pamoate) is unrelated chemically to the phenothiazines, reserpine, meprobamate, or the benzodiazepines.

Vistaril is not a cortical depressant, but its action may be due to a suppression of activity in certain key regions of the subcortical area of the central nervous system. Primary skeletal muscle relaxation has been demonstrated experimentally. Bronchodilator activity, and antihistaminic and analgesic effects have been demonstrated experimentally and confirmed clinically. An antiemetic effect, both by the apomorphine test and the veriloid test, has been demonstrated. Pharmacological and clinical studies indicate that hydroxyzine in therapeutic dosage does not increase gastric secretion or acidity and in most cases has mild antisecretory activity. Hydroxyzine is rapidly absorbed from the gastrointestinal tract and Vistaril's clinical effects are usually noted within 15 to 30 minutes after oral administration.

## INDICATIONS

For symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested.

Useful in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses, and in histamine-mediated pruritus.

As a sedative when used as premedication and following general anesthesia, **Hydroxyzine may potentiate meperidine (Demerol®) and barbiturates**, so their use in pre-anesthetic adjunctive therapy should be modified on an individual basis. Atropine and other belladonna alkaloids are not affected by the drug. Hydroxyzine is not known to interfere with the action of digitalis in any way and it may be used concurrently with this agent.

The effectiveness of hydroxyzine as an antianxiety agent for long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should reassess periodically the usefulness of the drug for the individual patient.

### CONTRAINDICATIONS

Hydroxyzine, when administered to the pregnant mouse, rat, and rabbit, induced fetal abnormalities in the rat and mouse at doses substantially above the human therapeutic range. Clinical data in human beings are inadequate to establish safety in early pregnancy. Until such data are available, hydroxyzine is contraindicated in early pregnancy.

Hydroxyzine pamoate is contraindicated for patients who have shown a previous hypersensitivity to it.

### WARNINGS

**Nursing Mothers:** It is not known whether this drug is excreted in human milk. Since many drugs are so excreted, hydroxyzine should not be given to nursing mothers.

### PRECAUTIONS

THE POTENTIATING ACTION OF HYDROXYZINE MUST BE CONSIDERED WHEN THE DRUG IS USED IN CONJUNCTION WITH CENTRAL NERVOUS SYSTEM DEPRESSANTS SUCH AS NARCOTICS, NON-NARCOTIC ANALGESICS AND BARBITURATES. Therefore, when central nervous system depressants are administered concomitantly with hydroxyzine, their dosage should be reduced. Since drowsiness may occur with use of the drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery while taking Vistaril (hydroxyzine pamoate). Patients should be advised against the simultaneous use of other CNS depressant drugs, and cautioned that the effect of alcohol may be increased.

### ADVERSE REACTIONS

Side effects reported with the administration of Vistaril are usually mild and transitory in nature.

**Anticholinergic:** Dry mouth.

**Central Nervous System:** Drowsiness is usually transitory and may disappear in a few days of continued therapy or upon reduction of the dose. Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually with doses considerably higher than those recommended. Clinically significant respiratory depression has not been reported at recommended doses.

### OVERDOSAGE

The most common manifestation of overdosage of Vistaril is hypersedation. As in the management of overdosage with any drug, it should be borne in mind that multiple agents may have been taken.

If vomiting has not occurred spontaneously, it should be induced. Immediate gastric lavage is also recommended. General supportive care, including frequent monitoring of the vital signs and close observation of the patient, is indicated. Hypotension, though unlikely, may be controlled with intravenous fluids and Levophed® (levarterenol) or Aramine® (metaraminol). Do not use epinephrine, as Vistaril counteracts its pressor action. Caffeine and Sodium Benzoate Injection, USP, may be used to counteract central nervous system depressant effects.

There is no specific antidote. It is doubtful that hemodialysis would be of any value in the treatment of overdose with hydroxyzine. However, if other agents such as barbiturates have been ingested concomitantly, hemodialysis may be indicated. There is no practical method to quantitate hydroxyzine in body fluids or tissue after its ingestion or administration.

### **DOSAGE**

For symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested: in adults, 50-100 mg q.i.d.; children under 6 years, 50 mg daily in divided doses and over 6 years, 50-100 mg daily in divided doses.

For use in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses, and in histamine-mediated pruritus: in adults, 25 mg t.i.d. or q.i.d.; children under 6 years, 50 mg daily in divided doses and over 6 years, 50-100 mg daily in divided doses.

As a sedative when used as a premedication and following general anesthesia: 50-100 mg in adults, and 0.6 mg/kg in children.

When treatment is initiated by the intramuscular route of administration, subsequent doses may be administered orally.

As with all medications, the dosage should be adjusted according to the patient's response to therapy.

### **HOW SUPPLIED**

Vistaril® Capsules (hydroxyzine pamoate equivalent to hydroxyzine hydrochloride)

25 mg:	100's (NDC 0069-5410-66), 500's (NDC 0069-5410-73), and Unit Dose (10 × 10's) (NDC 0069-5410-41) two-tone green capsules
50 mg:	100's (NDC 0069-5420-66), 500's (NDC 0069-5420-73), and Unit Dose (10 × 10's) (NDC 0069-5420-41) green and white capsules
100 mg:	100's (NDC 0069-5430-66), 500's (NDC 0069-5430-73), and Unit Dose (10 × 10's) (NDC 0069-5430-41) green and gray capsules

Vistaril® Oral Suspension (hydroxyzine pamoate equivalent to 25 mg hydroxyzine hydrochloride per teaspoonful-5 mL): 1 pint (473 mL) bottles (NDC 0069-5440-93) and 4 ounce (120 mL) bottles (NDC 0069-5440-97) in packages of 4.

Shake vigorously until product is completely resuspended.

#### **BIBLIOGRAPHY**

Available on request.

Pfizer Labs

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